SLEEP-DEPENDENT HYPERPROLACTINEMIA
AND CORPUS LUTEUM PATHOGENESIS

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Prolactin (PRL) secretion has been reported to be significantly increased under certain physiological conditions, basically due to an increment in the amplitude of sleep-induced secretion pulses 8. The same effect has been observed in tumor-induced or idiopathic hyperprolactinemia 1. High serum PRL levels may not modify the reproductive function in women, but can produce a wide variety of dysfunctions, including the amenorrhea-galactorrhea syndrome 2.

These alterations can be prevented by the administration of dopamine (DA) agonists. Since DA-agonist therapy has also been reported to be successful in some normoprolactinemic infertile women having an altered menstrual cycle 11, the aim of the present study was to investigate a hypothetical pathological PRL secretion pattern during sleep in this type of patients.

MATERIALS AND METHODS

Six women between 23 and 35 years of age with a diagnosis of sterility due to a luteal phase deficiency (LPD) were studied. The luteal phase deficiency was determined by at least two of the following parameters: a. endometrial biopsy, b. basal temperature and c. plasma progesterone serial determinations on appropriate days during the second half of the menstrual cycle.

Prolactin was assayed every 30 min for 12h (from 19th to 07th) in plasma samples obtained during the early follicular phase using an intravenous cath-

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SLEEP-DEPENDENT HYPERPROLACTINEMIA

In order to ensure a good adaptation of the patient, the catheter was inserted 3h prior to the first extraction. The catheter permeability between extractions was maintained by a physiological solution.

Five female volunteers with normal menstrual cycle and proved fertility were used as control group, employing the same extraction procedure and schedule as in the experimental group. In both groups sleep was physiological and none of the patients awoke during the sample extraction. All the women were adequately informed on the purpose of the study and all gave their consent.

PRL was measured by an already described double-antibody radioimmunoassay (RIA). Iodination was performed using hypochlorite as oxidant. Human PRL (75-504 preparation), used as a standard, was donated by MRC (Great Britain). Purified hypophysal human PRL used for iodination and the antibody (hPRL rabbit antiserum) were generously donated by NIAMDD-NIH (USA). The sheep anti-rabbit γ-globulin, used as a second antibody, was prepared in our laboratory. The assay sensitivity was 1.7 ng/ml and the intra- and inter-assay variation coefficients were 6.8 and 9.7%, respectively.

In order to avoid the inter-assay error, all samples from the same patient were evaluated in the same assay.

For statistical analysis, the following parameters were evaluated: 1. mean value and standard error of the mean (SEM) of PRL levels in wake conditions; 2. mean value and SEM of PRL plasma levels in sleep conditions; 3. all these values were calculated by the Student’s t test and p < 0.05 was considered as a statistically significant difference; 4. the highest amplitude pulse was considered as the difference between the mean values in sleep and wake states.

RESULTS

Figure 1 shows the PRL values obtained during wake and sleep in the control group. In all the patients there was a significant increase in PRL values during sleep. The sleep period lasted for between 04h and 06h. In relation to

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Fig. 1 - Twelve-h profile of serum PRL levels obtained in 5 normal women. Arrows indicate the total sleep periods.